E-2035

Comparative activity of ceftobiprole (BAL9141), daptomycin and linezolid *vs. S. aureus* from bacteremias in the UK and Ireland

E-mail: rreynolds@bsac.org.uk

R. Reynolds[1], D.M. Livermore[2], N. Potz[2], M. Colman[2], BSAC Working Party on Bacteraemia Resistance Surveillance[1]

[1]British Society for Antimicrobial Chemotherapy, Birmingham, B1 2JS [2]Health Protection Agency, London, NW9 5HT

Background

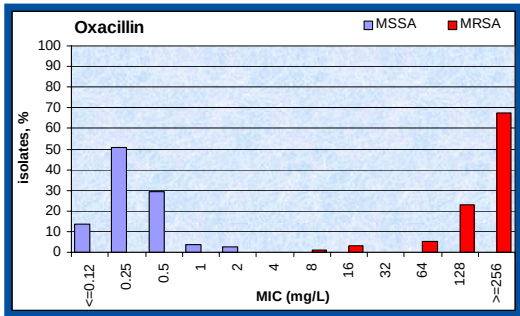
- Methicillin-resistant *S. aureus* cause 10% of bacteremias in the UK, and comprise 15% of all significant in-patient isolates. Such prevalence, in the UK and elsewhere, underlines the need for new anti-Gram-positive agents.
- Linezolid was launched in the UK in 2001.
- Daptomycin received FDA approval in 2003 but awaits a European license.
- The anti-MRSA cephalosporin ceftobiprole (BAL9141) is now in Phase III development.

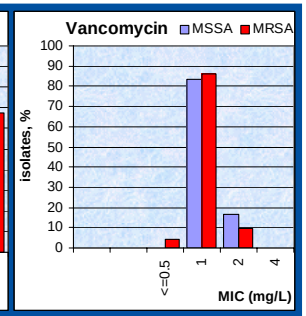
Methods

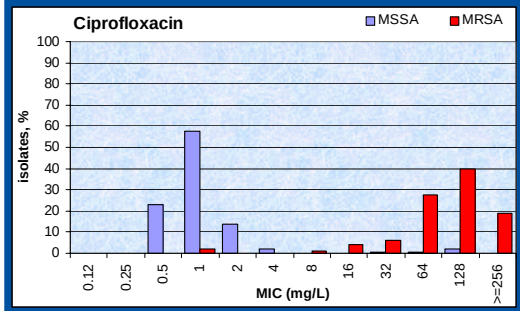
- The BSAC Bacteraemia Resistance Surveillance Programme (wwww.bsacsurv.org) collected 235 isolates of *S. aureus* from 25 laboratories in the UK and Ireland in 2003.
- MICs were measured centrally on Iso-Sensitest agar at 37°C for most agents, but on Columbia agar with 2%NaCl at 30°C for oxacillin.

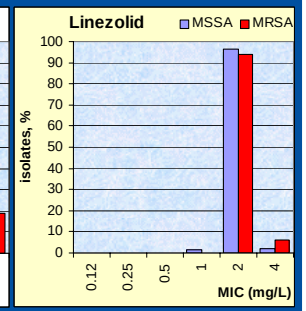
MSSA n = 140	MIC summary measures (mg/L)				geometric
	minimum	MIC_{50}	MIC_{90}	maximum	mean
oxacillin	≤0.12	0.25	0.5	1	0.3
ciprofloxacin	0.5	1	2	128	1.1
erythromycin	0.25	1	8	≥256	1.4
vancomycin	1	1	2	2	1.1
ceftobiprole	0.25	0.5	0.5	1	0.4
daptomycin	0.25	0.5	1	1	0.5
linezolid	1	2	2	4	2

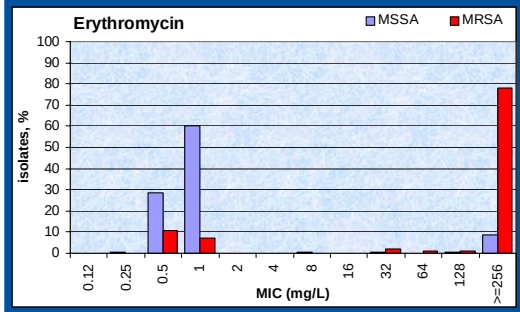
MRSA n = 95	MIC summary measures (mg/L)				geometric
	minimum	MIC_{50}	MIC_{90}	maximum	mean
ciprofloxacin	1	128	≥256	≥256	88.9
erythromycin	0.5	≥256	≥256	≥256	82.6
vancomycin	≤0.5	1	1	2	1
ceftobiprole	0.5	2	2	4	1.4
daptomycin	0.25	0.5	0.5	1	0.5
linezolid	2	2	2	4	2.1

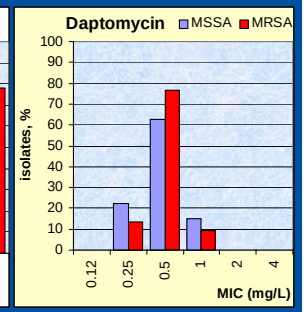












Results

- MIC distributions for 140 MSSA and 95 MRSA isolates are shown in the figures.
- Among MRSA, resistance to ciprofloxacin at 1 mg/L (98%) and erythromycin at 0.5 mg/L (89%) was widespread and high level (most MICs ≥64 mg/L). Such resistance is typical of the two prevalent UK epidemic clones, EMRSA-15 and -16.
- In MSSA, resistance to ciprofloxacin (19%) and erythromycin (71%) was mostly borderline (MICs 1-2 mg/L).
- No resistance to vancomycin, linezolid or daptomycin was seen, and no ceftobiprole MICs >4 mg/L.
- For vancomycin, linezolid and daptomycin, MIC distributions were tightly clustered and unimodal, with MRSA no less susceptible than MSSA.
- Ceftobiprole MICs were *ca.* 4-fold higher for MRSA than MSSA, and were further increased, though never >4 mg/L, on Columbia agar + 2% NaCl at 30°C (see poster E-2036).

Acknowledgements

Working Party Members (May 2004): A. MacGowan[1] (Chair), M. Allen[2], D. Brown[3], N. Deaney[4], I. Harding[5], R. Hope[6], D. Livermore[6], V. Reed[5], R. Reynolds[1], C. Thomson[7], A. White[8], R. Wiltshire[9]. **Organism ID and Susceptibility Testing:** M. Colman[6], N. Potz[6].

[1]North Bristol NHS Trust; [2]Wyeth; [3]Addenbrookes Hospital, Cambridge; [4]Merck, Sharp & Dohme; [5]Micron Research Limited; [6]Health Protection Agency, London; [7]Bayer Pharmaceuticals; [8]GlaxoSmithKline; [9]Pfizer.

Collecting Laboratories: *England*: William Harvey Hosp., Kent; Birmingham City Hosp.; Bristol Royal Infirmary; West Suffolk Hosp.; Addenbrooke's Hosp., Cambridge; Countess of Chester Hosp.; Coventry & Warwickshire Hosp.; Royal Infirmary, Leicester; St Mary's Hosp., London; University College Hosp., London; Wythenshawe Hosp., Manchester; Freeman Hosp., Newcastle; Northern General Hosp., Sheffield; Royal Shrewsbury Hosp.; Southampton General Hosp.; Sunderland Royal Hosp.; Treliske Hosp., Truro. *Ireland*: Cork University Hosp.; Beaumont Hosp., Dublin. *N. Ireland*: Belfast City Hosp.; Altnagelvin Area Hosp., Londonderry. *Scotland*: Glasgow Royal Infirmary; Victoria Hosp., Kirkcaldy. *Wales*: Ysbyty Gwynedd, Bangor; University Hosp. of Wales, Cardiff.

Central Laboratory: HPA, London.

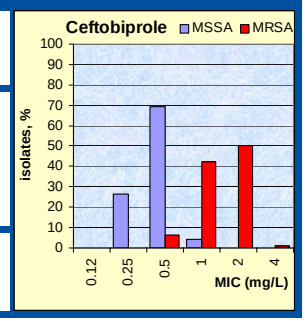
Sponsors: The BSAC Bacteraemia Resistance Surveillance Programme 2003 was sponsored by Cubist Pharmaceuticals, Merck Sharp and Dohme, Pfizer, and Wyeth, and supported by the BSAC. Basilea Pharmaceutica funded the testing of staphylococci with ceftobiprole.

Abbreviations
MSSA methicillin-susceptible *S. aureus*
MRSA methicillin-resistant *S. aureus*

Conclusion

Linezolid, daptomycin and ceftobiprole all show good activity against current MRSA from the UK and Ireland.

Correspondence to: Dr. R. Reynolds, Department of Medical Microbiology, Southmead Hosp., Bristol, BS10 5NB, England. **rreynolds@bsac.org.uk**



www.bsac.org.uk

ICAAC, Washington DC, 30 October - 2 November 2004, E-2035